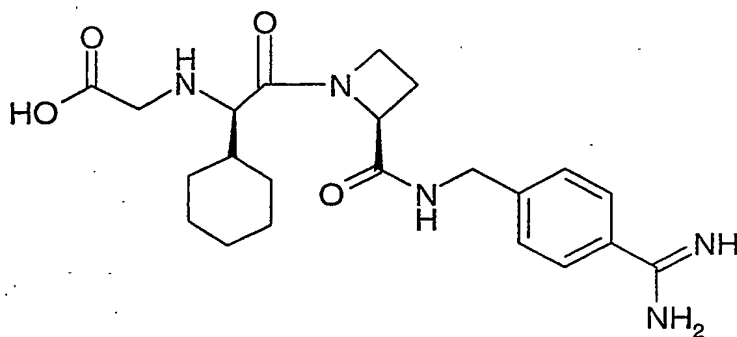
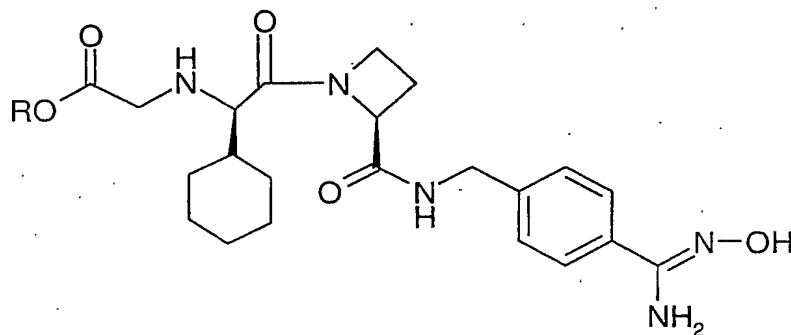


Claims

1. A process for the production of melagatran,

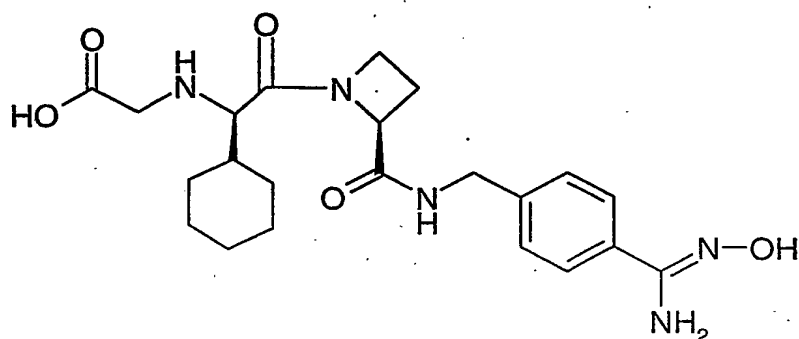


ex vivo, which process comprises the hydrolysis of a compound of formula I,



wherein R represents linear or branched C₁₋₆ alkyl or a benzylic group, to form, in substantially salt-free form, an intermediate compound of formula II,

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II

followed by reduction of that intermediate compound.

- 5 2. A process as claimed in Claim 1, wherein R represents linear or branched C₁₋₄ alkyl or a benzylic group.
3. A process as claimed in Claim 1 or Claim 2, wherein R represents methyl, ethyl, *n*-propyl, *i*-propyl or benzyl.
- 10 4. A process as claimed in any one of the preceding claims, wherein R represents ethyl.
5. A process as claimed in any one of the preceding claims, wherein
- 15 the hydrolysis step is carried out in the presence of a base.
6. A process as claimed in Claim 5 wherein the base is an alkali metal carbonate or an alkali metal hydroxide.
- 20 7. A process as claimed in Claim 6 wherein the base is potassium carbonate, sodium carbonate, lithium hydroxide, potassium hydroxide or sodium hydroxide.

8. A process as claimed in Claim 7 wherein the base is sodium hydroxide.
9. A process as claimed in any one of the preceding claims, wherein
5 the hydrolysis step is carried out in the presence of a lower alkyl alcohol, a diol, an ether and/or water as solvent.
10. A process as claimed in Claim 9, wherein the solvent is a mixture of a C₁₋₆ alkyl alcohol and water.
- 10 11. A process as claimed in Claim 10, wherein the alcohol is ethanol.
12. A process as claimed in any one of the preceding claims, wherein the hydrolysis step is carried out at between about 15°C and about 50°C.
- 15 13. A process as claimed in any one of the preceding claims, wherein preparative work up following the hydrolysis step involves acidification of the reaction mixture.
- 20 14. A process as claimed in Claim 13 wherein the acid that is added is sulphuric acid, phosphoric acid, hydrobromic acid or hydrochloric acid.
15. A process as claimed in Claim 13 or Claim 14 wherein the pH is adjusted to a weakly acidic value.
- 25 16. A process as claimed in Claim 15, wherein the pH value is pH 5 or thereabouts.

17. A process as claimed in any one of the preceding claims, wherein the reduction step is carried out by way of hydrogenation in the presence of a suitable catalyst system.

5 18. A process as claimed in Claim 17, wherein the catalyst is a precious metal.

19. A process as claimed in Claim 18, wherein the metal is platinum, ruthenium or palladium.

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20. A process as claimed in Claim 19, wherein the metal is palladium.

21. A process as claimed in any one of Claims 18 to 20 wherein the metal is provided on a support.

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22. A process as claimed in Claim 21 wherein the support is powdered charcoal.

23. A process as claimed in any one of Claims 17 to 22, wherein the
20 hydrogenation is carried out in the presence of a solvent system comprising a lower alkyl alcohol, water or a mixture thereof.

24. A process as claimed in Claim 23 wherein the alcohol is a C₁₋₆ alkyl alcohol.

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25. A process as claimed in Claim 24, wherein the alcohol is *i*-propanol, methanol or ethanol.

26. A process as claimed in any one of Claims 23 to 25 wherein the
30 solvent system is a mixture of methanol and water or ethanol and water.

27. A process as claimed in Claim 26 wherein the solvent system is a mixture of methanol and water in proportions of 70:30 (v/v) or thereabouts, or a mixture of ethanol and water in proportions of 62.5:37.5 (v/v) or thereabouts.

28. A process as claimed in any one of Claims 17 to 27 wherein the hydrogenation is carried out at elevated temperature.

29. A process as claimed in Claim 28, wherein the hydrogenation is carried out under a positive pressure of hydrogen.

30. A process as claimed in Claim 29, wherein the hydrogenation is carried out under at least 4 bar of hydrogen pressure.

31. A process as claimed in any one of Claims 17 to 30 wherein the hydrogenation is carried out in the absence of an inorganic acid, or an additional carboxylic acid, as part of the reaction mixture.